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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/917,384	07/28/2001	William S. Adney	NREL 01-38	9964

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	16

DATE MAILED: 08/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/917,384	Applicant(s) ADNEY ET AL.	
	Examiner Manjunath N. Rao, Ph.D.	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,14-25,28-35,44,45 and 69-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,14-25,28-35,44,45 and 69-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-11, 14-25, 28-35, 44-45, 69-74 are still at issue and are present for examination.

Applicants' amendments and arguments filed on 5-30-03, paper No.15, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 70 and claims 71-74 which depends therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 70 recites the phrase "substantially purified". The metes and bounds of the above phrase is not clear to the Examiner. It is not clear to the Examiner as to how much purity of the polypeptide is considered as "substantial purity". Examiner suggests cancellation of the phrase.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 14-25, 28-35, 44-45, 69-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a Gux I polypeptide comprising a catalytic domain with SEQ ID NO:5, further comprising a CBD-III domain with SEQ ID NO:4 and a

CBD-II domain with SEQ ID NO:7, or a peptide having SEQ ID NO:1 encoded by a nucleic acid sequence with SEQ ID NO:1, does not reasonably provide enablement for any or all such Gux I peptide comprising a catalytic domain of any 637 to about 643 amino acids in length or any CBDIII domain that is about 150-156 amino acids in length or any CBDII domain that is 95-105 amino acids in length or an amino acid sequence that is 90% identical to SEQ ID NO:1 or encoded by a polynucleotide that is 90% identical to SEQ ID NO:2, or a Gux1 peptide comprising a catalytic domain that is 70%, 80%, 90% to SEQ ID NO:5 and/or a CBD domain that is 90% identical to SEQ ID NO:7 or a peptide comprising amino acid sequence that is 70% or at least 90% identical to SEQ ID NO:4, 5, 6, 7 or 1 and fusion polypeptides of the above polypeptides comprising a heterologous polypeptide such a peptide tag, or a substrate targeting moiety or a composition comprising such polypeptides along with a carrier. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-5, 14-25, 28-35, 44-45, 69-74 are so broad as to encompass any glycosylhydrolase polypeptide comprising a catalytic domain of any 637 to about 643 amino acids in length or any CBDIII domain that is about 150-156 amino acids in length or any CBDII

domain that is 95-105 amino acids in length or an amino acid sequence that is 90% identical to SEQ ID NO:1 or encoded by a polynucleotide that is 90% identical to SEQ ID NO:2, or a Gux1 peptide comprising a catalytic domain that is 70%, 80%, 90% to SEQ ID NO:5 and/or a CBD domain that is 90% identical to SEQ ID NO:7 or a peptide comprising amino acid sequence that is 70% or at least 90% identical to SEQ ID NO:4, 5, 6, 7 or 1 and fusion polypeptides of the above polypeptides comprising a heterologous polypeptide such a peptide tag, or a substrate targeting moiety or a composition comprising such polypeptides along with a carrier.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of Gux1 polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one such Gux1 polypeptide with SEQ ID NO:1 encoded by SEQ ID NO:2. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides some even with an undefined function/activity. The specification is limited to teaching use of SEQ ID NO: 1 or a polypeptide comprising polypeptides with SEQ ID NO:4, 5 and 7 as a Gux1 polypeptide but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the

lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any glycosylhydrolase polypeptide as described in the above paragraphs because the specification does not establish: (A) regions of the protein structure which may be modified without effecting either the catalytic activity or the cellulose binding activity of the CBD domains; (B) the general tolerance of glycosylhydrolases such as cellulase or endoglucanases and the CBDs to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any glycosylhydrolase or any CBD polypeptide amino acid residues with an expectation of obtaining the desired biological function; and (D) the

specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including glycosylhydrolase catalytic domains, and cellulose binding domains with an enormous number of amino acid modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-5, 22-25, 69-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-5, 22-25, 69-74 are directed to composition comprising a Gux1 thermostable peptide wherein said Gux1 peptide comprises a catalytic domain GH48 of 637 to 643 amino acids in length, a carbohydrate binding domain CBD type III of 15-156 amino acids in length and a CBD type II of 95-105 amino acids in length and fusion polypeptides of the same fused to heterologous polypeptides. Claims 1-5, 22-25, 69-74 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides including modified polypeptide

sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue that have not been disclosed in the specification. No description has been provided of even a representative number of polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:1 or characterization of SEQID NO:4-7 as catalytic domains and CBD domains, has been provided by applicants which would indicate that they had possession of the claimed genus of all the polypeptides. The specification does not contain any disclosure of the structure of the polypeptide sequences, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicants have traversed the above rejection arguing that arguing that patents need not teach what is already well known in the art, that those skilled in the art would have the knowledge to modify the amino acid sequence with SEQ ID NO:1 and that such techniques for modification are well known. Applicants also recite from the *Amgen Inc. v. Hoechst Marion Rousel Inc.* case and the decision handed in that particular case.

Applicants also refer to the more recent *Enzo Biochem* case. While the Examiner has no objections to those decisions handed down by the courts, the same decisions cannot be extended to the instant claims and be argued that the above rejection needs to be withdrawn. Examiner has in fact rewritten the above rejection so that it makes it clear to the applicants as to why the above rejection has been applied. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genera of claims 1-5, 22-25, 69-74 includes species which are widely variant in structure. The genus of claims 1-5, 22-25, 69-74 is structurally diverse as it encompasses polypeptides with Gux1, glycosylhydrolase activity/cellulose binding activity from all or any source. As such, neither the

description of the function of the Gux1 polypeptide nor the disclosure solely of functional features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus. Hence the above rejection is maintained.

Claims 28-35, 44-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 28-35, 44-45 are directed to composition comprising an amino acid with SEQ ID NO:4, 5, 6, or 7 or polypeptides comprising amino acid sequences that are 70% identical to SEQ ID NO: 4, 5, 6, or 7 and fusion polypeptides comprising the above amino acid sequences. Claims 28-35, 44-45 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides whose function has not been described. No description has been provided of the all the polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:1 and 5 as a Gux1 polypeptide with a glycosylhydrolase activity or partial characterization of SEQID NO:4 and 7 as having cellulose binding activity, has been provided by applicants which would indicate that they had possession of the claimed genus of all the polypeptides. The specification does not contain any disclosure of the function of all the polypeptide sequences, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of function. Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification

discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicants have traversed the above rejection arguing that arguing that patents need not teach what is already well known in the art, that those skilled in the art would have the knowledge to modify the amino acid sequence with SEQ ID NO:1 and that such techniques for modification are well known. Applicants also recite from the *Amgen Inc. v. Hoechst Marion Rousel Inc.* case and the decision handed in that particular case. Applicants also refer to the more recent *Enzo Biochem* case. While the Examiner has no objections to those decisions handed down by the courts, the same decisions cannot be extended to the instant claims and be argued that the above rejection needs to be withdrawn. Examiner has in fact rewritten the above rejection so that it makes it clear to the applicants as to why the above rejection has been applied. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show

the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genera of claims 28-35, 44-45 includes species which are widely variant in function. The genus of claims 28-35, 44-45 is functionally diverse as it encompasses polypeptides comprising amino acid sequences that are 70% or 90% identical to SEQ ID NO:4-7 or 1 without any attached function to such polypeptides. As such, neither the description of the structure of one single Gux1 polypeptide (SEQ ID NO:1 or 5) or the CBD polypeptides (SEQ ID NO:4, 7), nor the disclosure solely of structural features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus. Hence the above rejection is maintained.

Conclusion

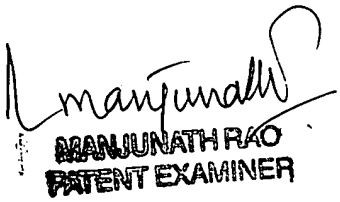
None of the claims are allowable.

Examiner has withdrawn the previous rejection of claims 14-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention, in view of the claim amendments.

Examiner has withdrawn the previous rejection of claims 1-3, 6-10, 14-25, 28-35, 44-45, 69-74 as obvious under 35 U.S.C. 103(a) over Zverlov et al. and Tomme et al. in view of the arguments presented by the applicants.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



Manjunath N. Rao
August 4, 2003